

61. The method as claimed in claim 38, using the structural protein in the form of an AAV particle, optionally in the form of an AAV capsid.

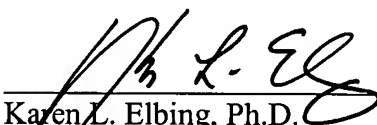
REMARKS

By this amendment, Applicants have replaced the original and amended set of claims with new claims 27-61, all of which find support in the original claim set. No new matter has been added.

If there are any other charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 5 March 2002

  
Karen L. Elbing, Ph.D.  
Reg. No. 35,238

Clark & Elbing LLP  
176 Federal Street  
Boston, MA 02110-2214  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



### PENDING CLAIMS

27. A method for purifying AAV and/or AAV particles by using a structural protein of adeno-associated virus (AAV), wherein the structural protein comprises at least one mutation which brings about an alteration in the chromatographic properties of the virus.
28. The method as claimed in claim 27, wherein the alteration in the chromatographic properties makes possible an improvement in the purification optionally selected from the group consisting of a concentration of the virus, preferably of the virus particles, to higher titers, a purification to greater purity, and a more efficient purification.
29. The method as claimed in claim 27, wherein the mutation brings about a negligible reduction in the infectivity of the virus.
30. The method as claimed in claim 27, wherein the mutated structural protein is capable of particle formation.
31. The method as claimed in claim 27, wherein the mutated structural protein increases the thermal stability.
32. The method as claimed in claim 27, wherein the structural protein is selected from the group consisting of mutated VP1, mutated VP2, and mutated VP3.

33. The method as claimed in claim 27, wherein the structural protein is derived from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, and other AAV serotypes derived therefrom.

34. The method as claimed in claim 27, wherein the mutation in the structural protein is selected from the group consisting of a point mutation, a mutation of more than one amino acid, one or more deletion(s), in particular one or more insertion(s), and a combination of said modifications.

35. The method as claimed in claim 27, wherein amino acids of a functional sequence, optionally suitable for affinity chromatography, are inserted into the structural protein.

36. The method as claimed in claim 35, wherein the inserted amino acid sequence is selected from the group consisting of a ligand of a receptor, the receptor of a ligand, an antibody, part of an antibody, in particular an antibody epitope, an antigen, an antigen epitope, a hormone, a hormone receptor, an enzyme, an enzyme substrate, a lectin, sugar-bearing amino acids, in particular from a histidine-rich peptide (His tag), a multiply charged peptide, glutathione S-transferase (GST tag), an F<sub>c</sub> part of an antibody, an immunoglobulin-binding domain, for example protein A or protein G or a part thereof, a lectin, a nucleic acid binding site, a heparin binding site, a specific ligand, a specific receptor, an integrin, a cytokine, a receptor binding domain of a cytokine, integrin,

growth factor, single-chain antibodies which bind to a cell surface receptor, an antibody against cell surface structures, an epitope, and an antibody-binding structure.

37. The method as claimed in claim 35, wherein a peptide which has the sequence QAGTFALRGDNPQG is inserted into the structural protein.

38. The method as claimed in claim 27, wherein the structural protein comprises at least one other mutation.

39. The method as claimed in claim 38, wherein the other mutation(s) in the structural protein bring(s) about an alteration in the infectivity of the virus.

40. The method as claimed in claim 38, wherein the other mutation(s) in the structural protein bring(s) about a reduction in the antigenicity of the virus.

41. The method as claimed in claim 38, wherein the other mutation(s) in the structural protein is/are selected from the group consisting of one or more deletion(s), one or more insertion(s), and a combination of said modifications.

42. The method as claimed in claim 38, wherein the insertion into the structural protein is selected from the group consisting of a cell membrane receptor ligand, a Rep protein, a Rep peptide, an immunosuppressive protein, an immunosuppressive peptide, a

protein with a signal for double strand synthesis of the foreign gene, and a peptide with a signal for double strand synthesis of the foreign gene.

43. The method as claimed in claim 38, wherein the insertion into the structural protein is selected from the group consisting of an integrin, a cytokine, a receptor binding domain of a cytokine, integrin, growth factor, single-chain antibodies which bind to a cell surface receptor, an antibody against cell surface structures, an antibody-binding structure, and an epitope.

44. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are located on the virus surface.

45. The method as claimed in claim 38, wherein the additional mutation(s) in the structural protein is/are located on the virus surface.

46. The method as claimed in claim 27, wherein the mutation(s) is/are located at the N terminus of the structural protein.

47. The method as claimed in claim 38, wherein the additional mutation(s) is/are located at the N terminus of the structural protein.

48. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are brought about by one or more insertions in the XhoI cleavage site of the VP1-encoding nucleic acid.

49. The method as claimed in claim 38, wherein the additional mutation(s) in the structural protein is/are brought about by one or more insertions in the XhoI cleavage site of the VP1-encoding nucleic acid.

50. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are brought about by one or more insertions in the BsrBI cleavage site of the VP1-encoding nucleic acid.

51. The method as claimed in claim 38, wherein the additional mutation(s) in the structural protein is/are brought about by one or more insertions in the BsrBI cleavage site of the VP1-encoding nucleic acid.

52. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are brought about by one or more deletions between the BsrBI-HindII cleavage sites of the VP1-encoding nucleic acid, and one or more insertions.

53. The method as claimed in claim 38, wherein the additional mutation(s) in the structural protein is/are brought about by one or more deletions between the BsrBI-HindII cleavage sites of the VP1-encoding nucleic acid, and one or more insertions.

54. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are brought about by one or more deletions between the XhoI-XhoI cleavage sites of the VP1-encoding nucleic acid.

55. The method as claimed in claim 27, wherein the additional mutation(s) in the structural protein is/are brought about by one or more deletions between the XhoI-XhoI cleavage sites of the VP1-encoding nucleic acid.

56. The method as claimed in claim 27, wherein the mutation(s) in the structural protein is/are brought about by one or more deletions between the BsrBI-HindII cleavage sites of the VP1-encoding nucleic acid.

57. The method as claimed in claim 38, wherein the additional mutation(s) is/are brought about by one or more deletions between the BsrBI-HindII cleavage sites of the VP1-encoding nucleic acid.

58. The method as claimed in claim 27, wherein one or more insertions in VP3 is/are located before and/or after at least one amino acid in the sequence selected from the group consisting of YKQIS SQSGA, YLTLN NGSQA, YYLSR TNTPS, EEKFF PQSGV, NPVAT EQYGS, LQRGN RQAAT, and NVDFV VDTNG.

59. The method as claimed in claim 38, wherein one or more additional insertion(s) in VP3 is/are located before and/or after at least one amino acid in the sequence selected from the group consisting of YKQIS SQSGA, YLTLN NGSQA, YYLSR TNTPS, EEKFF PQSGV, NPVAT EQYGS, LQRGN RQAAT, and NVDFT VDTNG.

60. The method as claimed in claim 27, using the structural protein in the form of an AAV particle, optionally in the form of an AAV capsid.

61. The method as claimed in claim 38, using the structural protein in the form of an AAV particle, optionally in the form of an AAV capsid.